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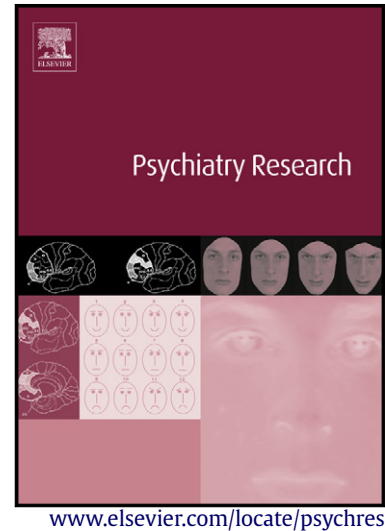
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## PSYCHIATRY RESEARCH

**Reliability and clinical correlates of the Astrand-Rhyming sub-maximal exercise test in patients with schizophrenia or schizoaffective disorder**

Davy Vancampfort<sup>a,b,\*</sup>, Hannes Guelinckx<sup>b</sup>, Marc De Hert<sup>b</sup>, Brendon Stubbs<sup>c</sup>, Andrew Soundy<sup>d</sup>, Simon Rosenbaum<sup>e,f</sup>, Els De Schepper<sup>b</sup>, Michel Probst<sup>a,b</sup>

<sup>a</sup>KU Leuven Department of Rehabilitation Sciences, Leuven, Belgium

<sup>b</sup>KU Leuven Department of Neurosciences, UPC KU Leuven, campus Kortenberg, Kortenberg, Belgium

<sup>c</sup>School of Health and Social Care, University of Greenwich, Eltham, London, UK

<sup>d</sup>Department of Physiotherapy, University of Birmingham, Birmingham, B15 2TT, UK

<sup>e</sup>School of Psychiatry, University of New South Wales, Sydney, Australia

<sup>f</sup>Musculoskeletal Division, The George Institute for Global Health and School of Public Health, University of Sydney, Sydney, Australia

\*Corresponding author. UPC KU Leuven, campus Kortenberg. Leuvensesteenweg 517, B-3070 Kortenberg, Belgium. Tel.: +32 2 758 05 11; Fax: +32 2 759 9879. *E-mail address:* [Davy.Vancampfort@uc-kortenberg.be](mailto:Davy.Vancampfort@uc-kortenberg.be) (D. Vancampfort)

### Abstract

Cardiovascular fitness is reduced in people with schizophrenia and is related to an increased morbidity and mortality. There is mounting interest in the accurate measurement of cardiovascular fitness in schizophrenia, yet existing measures used in the general population have not been tested on validity and reliability in this high-risk group. Therefore, we

examined the reproducibility and feasibility of the Astrand-Rhyming sub-maximal exercise test in patients with schizophrenia or schizoaffective disorder. Secondary aims were to assess minimal detectable changes, practice effects and the presence of clinical symptoms that are associated with cardio-respiratory fitness (expressed as estimated oxygen uptake). From 47 patients with schizophrenia or schizoaffective disorder two trials of the Astrand-Rhyming test, administered within three days, were analysed. The intraclass correlation coefficient for the estimated oxygen uptake between the two tests was 0.92 (95% confidence interval: 0.85 to 0.95). The minimal detectable change was 6.5mlO<sub>2</sub>/min/kg. No practice effect could be detected. A backward regression analysis demonstrated that illness duration, negative symptoms and level of physical activity explained 63.0% of the variance in estimated oxygen uptake. The current study demonstrates that the Astrand-Rhyming test can be recommended for evaluating the aerobic fitness in patients with schizophrenia or schizoaffective disorder.

**Keywords:** psychosis; aerobic fitness; physical activity

## 1. Introduction

In persons with schizophrenia or schizoaffective disorder, an impaired aerobic fitness is a major modifiable risk factor for cardiovascular disease and overall morbidity and mortality (Strassnig et al., 2011; Scheewe et al., 2012; Vancampfort et al., 2013a). For this reason, an impaired aerobic fitness is an important indicator for physical activity interventions within the multidisciplinary treatment of patients with schizophrenia (Stubbs et al., 2014; Uwakwe et al., 2014; Vancampfort et al., 2009, 2010). Given that physical activity might be beneficial in the prevention of cardiovascular diseases, support for aerobic exercise programmes in the multidisciplinary treatment of schizophrenia and schizoaffective disorder is growing (Scheewe et al., 2012, 2013; Strassnig et al., 2012; Vancampfort et al., 2012a, b).

Until recently, the promotion of aerobic fitness in patients with schizophrenia or schizoaffective disorder has received limited attention, in part due to lack of appropriate measures (De Hert et al., 2011; Vancampfort et al., 2011a). Laboratory-based incremental exercise testing protocols, that use breath-by-breath gas analysis and measure the maximum level of oxygen consumption ( $\text{VO}_{2\text{max}}$ ) are considered the ‘gold standard’ measurement of aerobic fitness (Vanhees et al., 2005). However, these test protocols are time-consuming, costly and need highly sophisticated equipment (Vanhees et al., 2005), which is often not available or practical in mental health care settings. Moreover, the maximal nature of the test may be influenced by the motivation of participants (Strassnig et al., 2011; Vancampfort et al., 2013b). Submaximal exercise tests that use measures of heart rate (HR) to estimate  $\text{VO}_{2\text{max}}$  are considered to be a reliable and valid measure of aerobic fitness (Lambrick, Faulkner, Rowlands, Eston, 2009). Importantly, for high-risk populations, submaximal tests are safer, better tolerated and consequently ideal for monitoring levels of aerobic fitness (Vanhees et al., 2005). A further benefit of submaximal testing is that it can allow greater numbers of patients to be longitudinally monitored at minimum costs. To date, there is no sub-maximal test which has been validated to assess the aerobic fitness of patients with schizophrenia.

One test which could be considered is the Astrand-Rhyming test (Astrand, 1960). The test utilizes a six minute, single stage, submaximal cycle ergometer protocol and is considered suitable for testing the general population (American College of Sports Medicine, 2013). Using this test, research (Nilsson et al., 2012; Ozbulut et al., 2013) has identified that patients with schizophrenia have a significantly lower aerobic fitness compared with age- and gender matched healthy controls. In order to validate these findings, help capture and reduce the burden of cardiovascular disease in individuals with schizophrenia, and further provide clinical practice a validated submaximal test of aerobic fitness, it is important that the

psychometric properties of the Astrand-Rhyming test are considered. Therefore, the aims of this study follow a series of iterative steps: (a) to investigate the test-retest reliability of the Astrand-Rhyming test in patients with schizophrenia or schizoaffective disorder, (b) to determine limits for the smallest difference in  $\text{VO}_2\text{max}$  that indicated a clinically meaningful change, (c) to explore whether there was a practice effect with repeated testing, (d) to assess clinical and demographic characteristics that might interfere with the test performance, and (e) to describe the feasibility of the test in patients with schizophrenia or schizoaffective disorder.

## **2. Methods**

### *2.1. Participants*

Over a 5-month period, inpatients with a DSM-V diagnosis of schizophrenia or schizoaffective disorder (American Psychiatric Association, 2013) admitted to the UPC KU Leuven in Belgium were invited to participate. Patients were excluded if they had a current co-morbid DSM-V diagnosis of substance abuse (American Psychiatric Association, 2013). The somatic exclusion criteria included evidence of significant cardiovascular, neuromuscular and endocrine disorders which, according to the American College of Sports Medicine (2013), might prevent safe participation in the study. All participants received a physical examination and baseline electrocardiogram before testing. Participants taking beta-blocking agents were excluded due to the potential influence on heart rate (HR) response. The study procedure was approved by the Scientific and Ethical Committee of the UPC KU Leuven, campus Kortenberg, Belgium in accordance with the principles of the Declaration of Helsinki. All participants gave their informed written consent. There was no compensation for participation in the study.

## 2.2. Sample size analysis

An a-priori sample size calculation was conducted. With a minimal acceptable intraclass correlation coefficient (ICC) of 0.80 and the hypothesis based on previous research (Vancampfort et al., 2011b; Vancampfort et al., 2012c) that present findings would be consistent with a minimum ICC of 0.90, a minimum sample size of 46 patients was required to attain a level of significance ( $\alpha$ ) of 0.05 and power of 0.8 ( $\beta = 0.2$ ) (Donner and Eliasziw, 1987; Walter et al., 1998). Considering previous reliability studies in patients with schizophrenia (Vancampfort et al., 2011b; Vancampfort et al., 2012c), it was anticipated that approximately 15% of patients would be excluded a-priori, approximately 15% would decline participation for motivational reasons and approximately 15% would dropout from the testing for motivational or other reasons. Therefore, a sample size around 75-80 participants was pre-specified to allow for these potential factors.

## 2.3. Study design

A test-retest design was used to test the reproducibility of the Astrand-Rhyming test (Astrand, 1960). Two tests were undertaken with the second test being repeated within three days by the same trained mental health physical therapist.

## 2.4. Astrand-Rhyming test

The Astrand-Rhyming protocol (Astrand, 1960) is a single-stage cycle ergometer test designed to elicit a steady-state heart rate over a 6-min period. The initial workload is selected from the Astrand test loading wattage table, pedaling speed remains constant (60 revolutions per min) and HR is recorded at every minute interval. The workload is set during the first 2 min and maintained throughout the test. In the case that HR fails to achieve the target zone, the load is adjusted accordingly. HR and loading wattage are noted at the end of each minute,

with a target goal of obtaining two consecutive HR values over 120 beats per minute (bpm), within 5 bpm of each other, during the fifth and sixth minute of work. The protocol was to be interrupted if threatening symptoms appeared or when the HR reached **85%** of age-predicted ( $220 - \text{age}$ ) maximum HR. Oxygen uptake ( $\text{VO}_2$ ) was estimated using the Astrand-Rhyming gender-sensitive nomogram (Astrand, 1960; American College of Sports Medicine, 2013). Results were then normalised to age.

### *2.5. Testing procedures*

The testing procedures were performed according to the American College of Sports Medicine guidelines (2013) in an indoor gym room with a minimum of external stimuli (e.g. no other participants present during the test). The therapist used a standardised instruction and language for each test and did not provide any verbal encouragement. Patients were requested to refrain from eating, drinking coffee or smoking during a two-hour period prior to the tests. At testing days medication was taken at the same hour of the day. Patients performed the retest at the same hour in standardised conditions. Blood pressure (BP) was before, during and after the test recorded with an Omron M6 (HEM-7001-E). HR was monitored continuously during testing by Polar HR monitors (Polar Heart Rate Monitor, Polar Oy, Kempele, Finland).

### *2.6. Psychosis evaluation tool for common use by caregivers (PECC)*

The PECC was used to assess schizophrenia symptoms (De Hert et al., 1998). The assessment was made prior to the first Astrand test by an independent mental health nurse. The assessor was blinded to all the other assessments and was provided with training on how to administer the PECC. The semi-structured PECC-interview evaluates 20 symptom items on a 7-point scale. Symptoms are grouped in 5 factors: positive, negative, depressive, cognitive and excitatory symptoms. The scores for each factor range from 4 to 28. Also extrapyramidal



side-effects of antipsychotic medication (EPS) were evaluated with the PECC-instrument. Scores range from 4 to 16. Higher scores indicate more severe side-effects. Validation results demonstrate that the PECC can be used for the evaluation of these symptoms and side-effects in schizophrenia or schizoaffective disorder (De Hert et al., 2002).

### *2.7. Physical activity participation*

The International Physical Activity Questionnaire (IPAQ) (Craig et al., 2003) was used to assess the level of physical activity. The IPAQ asks participants to recall activities for each of the last seven preceding days in morning, afternoon, and evening time periods. On the basis of what activities participants self-reported, the interviewer (blinded physical therapist) also clarified the perceived intensity of that specific activity. A continuous indicator was calculated as a sum of weekly metabolic equivalent (MET)-minutes per week of physical activity. The MET energy expenditure was estimated by weighting the reported minutes per week by a MET energy expenditure estimate for each type of activity (low, moderate and vigorous intensity physical activity). The weighted MET-minutes per week were calculated as duration x frequency per week x MET-intensity, which were then summed to produce a weighted estimate of the total physical activity from all reported activities per week as per the IPAQ scoring protocol. Previous research indicated that the IPAQ can be considered as a reliable surveillance tool to assess levels of physical activity in patients with schizophrenia (Faulkner et al., 2006).

### *2.8. Medication use*

**Antipsychotic medication was recorded** for each patient and converted into a daily equivalent dosage of chlorpromazine according to consensus by Gardner et al. (2010). Data on the use of medication was obtained from patients' medical records.

### 2.9. Other clinical variables

Body weight was measured by the (blinded) research nurse in light clothing to the nearest 0.1 kg using a SECA beam balance scale, and height to the nearest 0.1 cm using a wall-mounted stadiometer. Illness duration and data on physical co-morbidity were obtained from patients' medical records. Metabolic syndrome was assessed using the International Diabetes Federation criteria (Alberti et al., 2006).

### 2.10. Statistical analyses

Descriptive statistics are presented as mean  $\pm$  standard deviation (SD). In order to assess the reliability between the two Astrand-Rhyming tests, the intraclass correlation coefficient (ICC) and its associated 95% confidence interval (CI) of the oxygen uptake estimates between the two Astrand-Rhyming tests were calculated using a one-way random single measures intraclass correlation analysis.

The minimal detectable change (MDC) for was calculated by multiplying the standard error of measurement (SEM) by 1.96 to correspond to the 95% CI and the square root of two to adjust for sampling from two different measurements. The SEM was estimated as the pooled standard deviation (SD) of pre-test and post-test assessments multiplied by the square root of (1-ICC) (de Vet et al., 2006). The SEM quantifies the within-subject variability and takes the amount of measurement errors into consideration. MDC<sub>95</sub> means one can be 95% confident that a change score equal or exceeding this threshold is true and reliable and not just a measurement error (Portney and Watkins, 2009).

To assess whether there was a practice effect with repeated testing, the four following methods were used. First, the ICC was interpreted. An ICC of less than 0.75 for the two successive tests was indicative of a practice effect (Portney and Watkins, 2009). The second

method was a Pearson correlation ( $r$ ) of less than 0.75 between successive trials. When the  $r$ -value equals 1, there is perfect agreement between both trials, and the Pearson correlation and the ICC concur in value. The third method was a statistically significant ( $P < 0.05$ ) improvement in the mean Astrand-Rhyming test scores between two trials, evaluated with a paired T-test and expressed with the 95% CI. The fourth method was the Bland-Altman method illustrating the means and the differences in oxygen uptake estimates of the Astrand-Rhyming tests for each subject (Bland and Altman, 2007). A  $P$ -value for the Spearman rank correlation coefficient between the means and the differences in oxygen uptake estimates of less than 0.05 indicates that the magnitude of the difference in oxygen uptake at baseline varies by the level of aerobic fitness. Because previous studies have not operationally defined practice effects and no single method of evaluation has been identified as superior to the others, the present study considers in parallel with a previous study in patients with schizophrenia (Vancampfort et al., 2011b) that a practice effect was to be present only if all four criteria have been fulfilled.

Pearson correlations were used to compute associations between the oxygen uptake estimates and demographical data and other variables. To identify independent predictors of the estimated oxygen uptake oxygen uptake ( $\text{VO}_2$ ) obtained on the second trial, a backward regression analysis including all significant correlates was conducted. A priori, a level of significance was set at  $P < 0.05$ .

Statistical analysis was performed using the statistical package SPSS version 22.0 (SPSS Inc., Chicago, IL).

### 3. Results

#### 3.1. Participants

Out of 77 patients with schizophrenia or schizoaffective disorder, 66 met the inclusion criteria of which 19 declined to participate ( $n=15$ ) or dropped-out ( $n=4$ ). Reasons for exclusion and drop-out are presented in Figure 1. The gender distribution of the final included sample was 34 men ( $34.1 \pm 12.0$  years;  $BMI=25.4 \pm 3.2$ ) and 13 women ( $34.3 \pm 9.2$  years;  $BMI=27.1 \pm 6.6$ ). Age ranged from 20 to 62 years. Seventy-six percent of the patients ( $n=36$ ) smoked. All individuals were Caucasians, and all except two were treated with antipsychotic drugs at the moment of the assessments. An overview of the medication intake is presented in Table 1. Mean daily equivalent dosage of chlorpromazine ( $n=45$ ) was  $678.5 \pm 394.9$  mg/day. Physical co-morbidity of the included patients is presented in Table 2. In summary, the most common co-morbid conditions were respiratory diseases, cardiovascular diseases, locomotor disorders, diabetes and the metabolic syndrome.

#### 3.2. Astrand-Rhyming test scores in schizophrenia or schizoaffective disorder

The mean estimated  $VO_2$  on the first and second test were respectively  $34.6 \pm 8.7$  mlO<sub>2</sub>/min/kg and  $34.5 \pm 8.7$  mlO<sub>2</sub>/min/kg. When looking at the mean oxygen consumption at steady state of both tests, it was noticed that there was no gender difference in  $VO_2$  ( $35.3 \pm 8.6$  mlO<sub>2</sub>/min/kg in men versus  $32.1 \pm 9.0$  mlO<sub>2</sub>/min/kg in women,  $P=0.29$ ).

#### 3.3. Reliability and minimal detectable changes of the Astrand-Rhyming test

Analyses of reproducibility of the Astrand-Rhyming test showed that the ICC for the whole sample was 0.92 with a 95% CI of 0.85-0.95. The  $MDC_{95}$  in the present study was 6.5 mlO<sub>2</sub>/min/kg.

### 3.4. Determination of a practice effect

The correlation between Astrand-Rhyming test scores at trial one and two was 0.91 ( $P<0.001$ ). A  $r^2$  value of 0.835 indicated that the performance on trial one explained 83.5% of the variability in the trial two performance. The  $\text{VO}_2$  on the second trial was not significantly different to the  $\text{VO}_2$  obtained on the first trial ( $P=0.79$ ). The Bland-Altman plot in figure 2 showed no significant pattern between the mean  $\text{VO}_2$  scores and differences in  $\text{VO}_2$  scores at the individual level, and this was supported by a Spearman rank correlation coefficient of -0.08 with a  $P$ -value of 0.59. The plot revealed one outlier: a male participant (23 years old, BMI=22.1) who had an estimated  $\text{VO}_2$  of 40ml  $\text{O}_2/\text{min}/\text{kg}$  based on a workload of 125 Watt and a mean steady state HR of 139bpm (at min five and six) at the first trial showed a steady state HR of 157 bpm at a same workload on the second trial, which corresponds with a  $\text{VO}_2$  of 32ml  $\text{O}_2/\text{min}/\text{kg}$ . As expected, 95% of the differences were within 2 SDs of the mean.

### 3.5. Variables associated with the Astrand-Rhyming test

Table 3 shows that age ( $P=0.043$ ), illness duration ( $P=0.003$ ), BMI ( $P<0.001$ ), negative ( $P=0.004$ ), depressive ( $P=0.005$ ), cognitive ( $P=0.001$ ) symptoms and extrapyramidal side-effects ( $P=0.006$ ) were negatively associated with the estimated oxygen uptake. Higher levels of physical activity ( $P<0.001$ ) was positively associated with oxygen uptake.

All significant correlates were included in a backward regression analysis with the estimated oxygen uptake as the dependent variable. Within the fully adjusted model, the largest unique significant predictor of oxygen uptake was physical activity levels ( $\beta=0.48$ ,  $p<0.001$ ), followed by illness duration ( $\beta=-0.31$ ,  $p<0.001$ ) and negative symptoms ( $\beta=-0.22$ ,  $p=0.034$ ). The model explained 63.0% of the variance in estimated oxygen uptake.

## 4. Discussion

### 4.1. Reliability and minimal detectable changes

This is the first study investigating the reliability of the Astrand-Rhyming sub-maximal exercise test in patients with schizophrenia or schizoaffective disorder. Our findings demonstrate that this sub-maximal aerobic test is both highly reproducible and reliable. With the mounting calls to reduce the increased mortality due to cardiovascular disease in people with schizophrenia, our results demonstrate promise and suggest that the Astrand-Rhyming test can be suitably used to monitor aerobic fitness in this population.

Interpreting change scores and identifying clinically significant changes in performance have become an explicit focus of the rehabilitation profession in mental health care settings (Vancampfort et al., 2012d). Clinicians are encouraged to understand how changes in scores translate to clinical relevance. The present study calculated the  $MDC_{95}$ , which provides meaningful criteria for assessing performance changes. A  $MDC_{95}$  of  $6.5 \text{ mlO}_2/\text{min/kg}$  implies that greater changes in oxygen uptake than these values are necessary on the Astrand-Rhyming test in order to be 95% certain that the changes are not due to measurement error or patient variability. Previous research in patients with schizophrenia demonstrated that such changes in oxygen uptake are achievable after a 6-week, 3 times a week 30min cardiovascular exercise programme (Strassnig et al., 2012).

The treatment of schizophrenia should therefore target improvement of aerobic fitness. This study adds to current knowledge that the oxygen uptake as assessed with the Astrand-Rhyming test could be a clinically relevant outcome measure.

### 4.2. Practice effects

Since the ICC and the correlation between both estimated  $\text{VO}_2$  scores were higher than 0.75, the *P*-value of the Spearman correlation between the means and differences in Astrand-

Rhyming test scores was higher than 0.05 and the  $\text{VO}_2$  at the second trial was not significantly different compared with the first, a practice effect can be excluded. The present study therefore indicates that a habituation test should not be recommended to offset any practice effects.

#### *4.3. Factors associated with the Astrand-Rhyming test performance*

The backward regression analysis demonstrated that longer illness duration and more severe negative symptoms might explain a lower aerobic fitness. Previous research on physical activity correlates in patients with schizophrenia and schizoaffective disorder showed that longer illness duration and more severe negative symptoms are associated with a sedentary lifestyle and lack of physical activity (Vancampfort et al., 2012e; Vancampfort et al., 2013a). Associations between negative symptoms and impaired aerobic fitness have been reported before in this population (Scheewe et al., 2013). However in contrast, Strassnig et al. (2011) found that aerobic fitness was only associated with the severity of positive symptoms and not with negative symptoms. More longitudinal and interventional research therefore is needed before firm conclusions related to any associations between psychiatric symptoms and aerobic fitness in patients with schizophrenia or schizoaffective disorder can be made. Unsurprisingly, the largest unique predictor of oxygen uptake was higher levels of physical activity participation, highlighting the importance of promoting activity in people with schizophrenia. The observation that antipsychotic medication use was not associated with a lower aerobic fitness is in accordance with previous research (Scheewe et al., 2013). The current data therefore indicates that the exposure to an unhealthy lifestyle rather than to antipsychotic medication use is associated with a worse performance on aerobic exercise tests. However, more longitudinal and interventional research is needed before any firm conclusions can be drawn.

#### *4.4. Feasibility*

The current study demonstrates that with an appropriately standardised method, the Astrand-Rhyming test is highly reproducible in patients with schizophrenia or schizoaffective disorder facing motivation problems when performing physical activities (Vancampfort et al., 2013b). Only one test had to be terminated prematurely due to leg fatigue. Given present observations and its safety profile based on other studies in high-risk patients tested without complications (Lennon et al., 2012; Speelman et al., 2012; Thorsen et al., 2009), there appears to be no reason why physician attendance is required. In order to guarantee maximal safety, we recommend that the Astrand-Rhyming test is supervised by an experienced clinician (e.g., a mental health physical therapist) and should preferably be conducted in a setting which has medical cardiopulmonary resuscitation training expertise within a near proximity and on the same site location. The fact that no practice effects were observed has also important clinical implications since repeated tests are often cumbersome to implement in clinical trials and are less cost effective in clinic settings.

#### *4.5. Study limitations*

An important limitation of the present study is that it included only a sample of inpatients from one specific centre while it was pre-dominantly based on data obtained from male participants. This may affect the ability to generalise present results. However, the sample size was adequately powered and calculated a-priori. Despite these limitations, the present study clearly demonstrates that the Astrand-Rhyming sub-maximal exercise test is a reliable and feasible test to assess the aerobic fitness in patients with schizophrenia or schizoaffective disorder. Because it is easy to perform, safe and inexpensive, the test could be used in daily mental health care. Since we did not find any evidence for a practice effect, the elimination of a habituation trial will save time and reduce participant's fatigue. The identification of a



minimal detectable change of 6.5mlO<sub>2</sub>/min/kg supports the use of the Astrand-Rhyming sub-maximal exercise test to identify patient-important change in research and clinical practice.

### **Contributors**

The study was designed by D Vancampfort, M De Hert and M Probst. All data were collected by H Guelinckx and E De Schepper. Statistical analyses were performed by D Vancampfort and M Probst. D Vancampfort and M Probst wrote the first draft of the paper, all other co-authors commented and contributed to the subsequent revisions. All authors have approved the final manuscript.

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**Table 1** Medication use in assessed patients with schizophrenia or schizoaffective disorder ( $n = 47$ ).

No antipsychotic	3 (6.4%)
Monotherapy antipsychotic	
Amisulpride	3 (6.3%)
Aripiprazole	2 (4.2%)
Bromperidol	1 (2.1%)
Clotiapine	1 (2.1%)
Clozapine	4 (8.5%)
Quetiapine	2 (4.2%)
Olanzapine	8 (17.0%)
Paliperidone	9 (19.1%)
Combination of antipsychotics	
Second-generation	11 (23.4%)
First- and second generation	4 (8.5%)
Other medication	
Anticholinergic	3 (6.3%)
Antidepressant	15 (31.9%)
Benzodiazepine	10 (21.3%)
Mood stabiliser	7 (14.9%)
Somatic medication	12 (25.5%)

**Table 2** Physical co-morbidity\* in assessed patients with schizophrenia ( $n = 47$ ).

Respiratory tract diseases	4 (8.5%)
Cardiovascular diseases	4 (8.5%)
Thyroid diseases	1 (2.1%)
Locomotor disorders	4 (8.5%)
Viral diseases	1 (2.1%)
Skin and connective tissue diseases	2 (4.2%)
Metabolic Syndrome <sup>°</sup>	18 (38.3%)
Diabetes	4 (8.5%)

\*Based on medical records; <sup>°</sup>According to International Diabetes Federation criteria (Alberti et al., 2005).



**Table 3**

Clinical characteristics for the experimental group ( $n = 47$ ) and Pearson Rho correlations with the estimated oxygen uptake on the second trial.

	Mean $\pm$ SD	Correlation with VO <sub>2</sub>	<i>P</i>
Age (years)	34.2 $\pm$ 11.2	-0.30	0.043*
Illness duration (years)	12.5 $\pm$ 11.6	-0.42	0.003*
BMI (kg/m <sup>2</sup> )	25.8 $\pm$ 4.3	-0.53	<0.001*
Chlorpromazine eq (mg/day)	649.6 $\pm$ 410.3	-0.28	0.055
Smoking (cigarettes/day)	13.1 $\pm$ 11.8	-0.025	0.87
PECC positive symptoms	9.2 $\pm$ 4.3	-0.20	0.18
PECC negative symptoms	9.7 $\pm$ 4.1	-0.41	0.004*
PECC depressive symptoms	9.5 $\pm$ 4.0	-0.41	0.005*
PECC excitatory symptoms	8.2 $\pm$ 3.7	0.047	0.75
PECC cognitive symptoms	7.9 $\pm$ 4.1	-0.48	0.001*
PECC extrapyramidal side-effects	5.1 $\pm$ 1.1	-0.40	0.006*
IPAQ total (MET-min/week)	785.7 $\pm$ 508.5	0.69	<0.001*

VO<sub>2</sub>=estimated oxygen uptake, BMI=body mass index, eq=equivalent, PECC=Psychosis Evaluation Tool for Common Caregivers, IPAQ=International Physical Activity Questionnaire, MET=metabolic equivalent; Significant when  $P<0.05$ .

**Table 4**

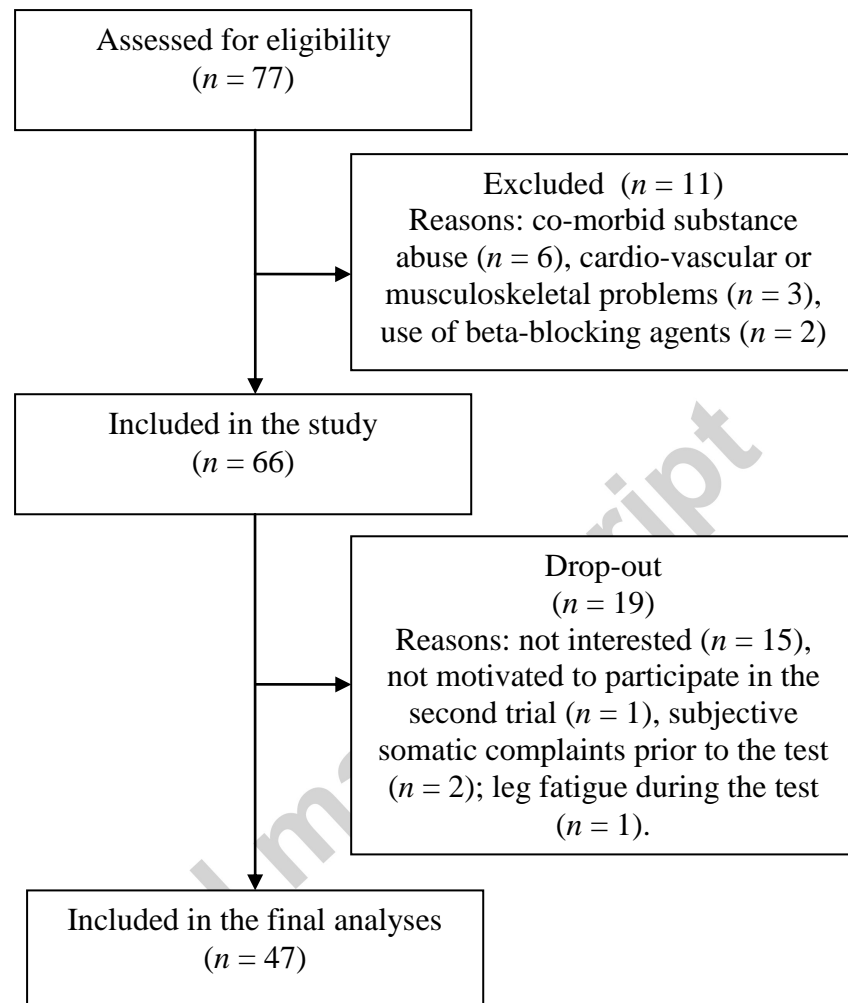
A backward regression model<sup>o</sup> with the estimated oxygen uptake as the dependent variable

Model	Unstandardised coefficients		Standardised coefficients $\beta$	t	P
	B	SE			
(Constant)	42.1	4.3		9.7	<0.001*
Illness duration (years)	-0.24	0.07	-0.31	-3.2	0.002*
PECC Negative symptoms	-0.46	0.21	-0.22	-2.2	0.034*
PECC Extrapyramidal side-effects	-1.31	0.78	-0.17	-1.7	0.097
IPAQ total (MET-min/week)	0.008	0.002	0.48	5.0	0.001*

<sup>o</sup>All significant correlates were originally included in the model. The adjusted  $r^2$  for the final model= 0.63. SE=standard error, PECC=Psychosis Evaluation Tool for Common Caregivers, IPAQ=International Physical Activity Questionnaire, MET=metabolic equivalent, \*significant when  $P<0.05$ .

**Figure 1**

Flowchart of the eligible patients



**Figure 2**

Agreement assessment (Bland-Altman plot) of the Astrand-Rhyming test between time 1 (t1) and time 2 (t3) ( interval maximum 3 days) in patients with schizophrenia or schizoaffective disorder.

